

Remarks

Introduction

✓ This Amendment and Reply addresses issues raised in the Office Action dated March 11, 2009. Claims 1-7 are pending in the application. Claims 1-3, 6 and 7 stand rejected. Claims 4 and 5 stand objected to. No new matter is presented. Consideration of the remarks presented herein is respectfully requested.

Objection to Abstract

The Examiner objects to the abstract as not being presented in the proper domestic form. With the present Reply and Amendment, Applicants amend the abstract as set forth on page 2 of this submission. Applicants respectfully request withdrawal of the objection in view of the amendments presented herein.

Rejection of claims 1-3, 6 and 7 under §103(a)

Claims 3-6 are rejected under 35 U.S.C §103(a) as being unpatentable over Linn et al. (US Patent No. 5,169,839) in view of Albers-Schonberg et al. (U.S. Patent No. 4,310,519). The Examiner contends that it would have been obvious to a person having ordinary skill in the art at the time the claimed invention was made to modify the compounds disclosed by Linn et al. (U.S. Patent No. 5,169,839 - i.e., compounds in column 2 showing antiparasitic activity having R₆ which is a loweralkoxymethoxy group, provided that R₄ and R₅ cannot be methyl at the same time) in combination with the teaching of Albers-Schonberg et al. (U.S. Patent No. 4,310,519 - i.e., avermectins having antiparasitic activity wherein both R₄ and R₅ groups are methyl groups). The Examiner reasons that such compounds are obvious because such a person would have expected the resulting compounds to possess antiparasitic activity. Applicants respectfully traverse the rejection for the following reasons.

The question of obviousness is resolved on the basis of underlying factual determinations including (1) the scope and content of the prior art, (2) any differences between the claimed subject matter and the prior art, (3) the level of skill in the art. *KSR Intl Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). Stark differences exist between the instantly claimed compounds and those disclosed by Linn et al. and Albers-Schonberg et al. such that a rejection under §103 cannot be properly maintained. The primary reference, Linn et al., discloses derivatives of avermectin

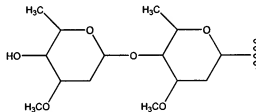
compounds wherein one or both of the 13-oleandrose saccharide groups lack a methyl group at the 3'- or 3"-methoxy which corresponds to the positions labeled as R4 and R5, respectively.

Specifically, Linn et al. disclose:

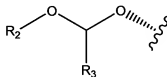
R4 and R5 are independently hydrogen, methyl, loweralkanoyl, benzoyl, loweralkoxycarbonyl, phenoxycarbonyl, carbamoyl, N-loweralkylcarbamoyl, N,N-diloweralkyl-carbamoyl or loweralkoxy loweralkyl., provided that both R4 and R5 are hydrogen only when R6 is other than hydroxyl and provided that both R4 and R5 are not simultaneously methyl.

(emphasis added)(column 2, lines 37 – 44).

The instantly claimed compounds recite a methyl at both of the positions referred to as "R4" and "R5" in Linn et al. (when n is 1 in both the instant claim 1. Thus, the instantly claimed compounds disclosed differ substantially from that of Linn et al. due to the above-recited limitation set forth by Linn et al. Further, Albers-Schonberg et al. disclose compounds that are produced by the fermentation of a nutrient medium with *Streptomyces avermitilis*. While Albers-Schonberg et al. disclose methyl groups at the R4 and R5 position, the disclosed compounds differ substantially from the instantly claimed compounds at the substituent disclosed by Albers-Schonberg et al. at the "R" position (the position labeled as "ε" in the instant claim 1). Specifically, Albers-Schonberg et al. disclose compounds where the "R" must be the following substituent:



In contrast, the instantly claimed compounds require the following substituent at the same position:

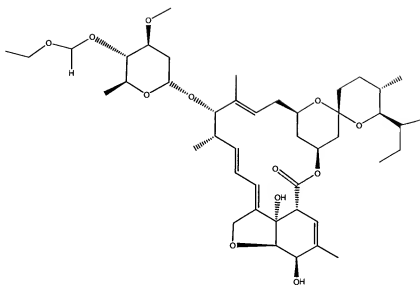


For a chemical compound, a *prima facie* case of obviousness requires structural similarity between the claimed compound and that of the prior art where the prior art gives reason or motivation to

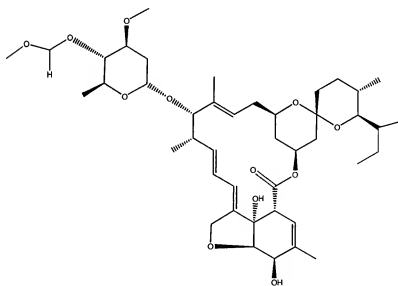
make the claimed compound or compositions. See *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007); *Yamanouchi Pharmaceutical Co., Ltd v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000). In the instant case, the Examiner has not only failed to show how the prior art gives reason or motivation to make the claimed compound but has failed to provide the requisite articulated reasoning with a rational underpinning to support the legal conclusion of obviousness in view of the articulated differences between the instantly claimed compounds and those of the cited prior art. Thus, Applicants respectfully request withdrawal of the rejection under §103 for this reason.

Secondly, the Examiner appears to presume that the combined teachings provide a basis for one of ordinary skill to have arrived at the instantly claimed compounds. The Federal Circuit has held that the presumption of obviousness based on a reference disclosing structurally similar compounds may be overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar compounds. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978). The instantly claimed compounds show an improvement of the activity of the class of insecticide/acaricide compounds through optimizing the recited substitution pattern. To illustrate both the impact of structural differences on performance as well as the superior properties of the claimed compounds based on the substitution pattern, compounds 3.5 & 3.6 (see compounds 3.5 & 3.6 page 26 paragraph [0200] of US 2006/0148729 A1) of the present invention were tested under standardized tests conditions using identical test methods (see methods described *infra*).

Applicants note that the only structural difference between compounds 3.5 & 3.6 resides in the presence of an ethyl group at position R₂ for compound 3.5 & of a methyl group at position R₂ for compound 3.6 as illustrated in the structures below:



Compound 3.5



Compound 3.6

The test methods used to conduct the experiment were as follows:

Frankliniella occidentalis on bean

Bean plants were treated in a spray chamber with diluted test solutions. After drying, the infestation was mixed with the population. Twelve days after the infestation, samples are checked for reduction of treated population and compared to the non-treated population.

Tetranychus urticae on bean:

Bean plants were infested with a mixed population. One day after infestation, the plants were treated in a spray chamber with diluted test solutions. One and ten days later, samples are checked for egg mortality, larval mortality, and adult mortality.

Heliothis virescens on cotton:

Cotton (*Gossypium barbadense*) leaf discs were treated via potter tower spray application. After drying, the infestation was implemented with ten L1 larvae per disc. Six days after infestation, samples are checked for larval mortality and larval growth effects.

Spodoptera littoralis on cotton:

Cotton (*Gossypium barbadense*) leaf discs were treated via potter tower spray application. After drying, the infestation was implemented with ten L1 larvae per disc. Six days after infestation, samples are checked for larval mortality and larval growth effects.

Spodoptera littoralis on cotton, persistence:

Cotton (*Gossypium barbadense*) plants were treated in a spray chamber with diluted test solutions. After application, plants are incubated in a green house. Treated leaves were fed to L3 larvae at different points in time including two, ten, and sixteen days after application. The cotton plants were assessed for larval mortality and larval growth effects six days after treated leaves fed to L2 larvae.

The test results are summarized in the following table:

Test	Method Name			Compound No 3.5	Compound No 3.6
<i>Frankliniella occidentalis</i> on bean	frocMpphs/con-P-I	mixed population mortality		0.8 ppm	0.8 ppm
<i>Tetranychus urticae</i> on bean	teurMpphs/con-P-I	egg mortality	1 day	n.a.	n.a.
			10 days	>0.2 ppm	>3 ppm
		larval mortality	1 day	0.05 ppm	0.05 ppm
			10 days	0.2 ppm	<0.01 ppm
		adult mortality	1 day	0.05 ppm	<0.01 ppm
			10 days	0.1 ppm	<0.01 ppm
<i>Heliiothis virescens</i> on cotton	hevil1gos/pot-S-I	larval mortality		12.5 ppm	0.8 ppm
<i>Spodoptera littoralis</i> on cotton	splil1gos/pot-S-I	larval mortality		0.8 ppm	<0.2 ppm
<i>Spodoptera littoralis</i> on cotton	splil3gos/fco-S-I	larval mortality	2 days	>12.5 ppm	12.5 ppm
			10 days	>12.5 ppm	12.5 ppm
			16 days	>12.5 ppm	12.5 ppm
		larval growth effects	2 days	12.5 ppm	0.8 ppm
			10 days	>12.5 ppm	3 ppm
			16 days	12.5 ppm	12.5 ppm

In summary, the two compounds exhibited comparable activities against thrips (*Frankliniella occidentalis*), but compound 3.6 exhibited clearly superior activity against spider mites (*Tetranychus urticae*) and the Lepidoptera species *Heliiothis virescens* and *Spodoptera littoralis*. Applicants contend that there is no incentive for a skilled person knowing the above-mentioned prior art documents to replace an ethyl group at position R₂ by a methyl group with a reasonable expectation of achieving a strong improvement of the insecticidal activity. Further, Applicants submit that the presumption of obviousness based on a reference allegedly disclosing structurally similar

compounds is overcome based on the evidence presented herein which shows there is no reasonable expectation of similar properties in structurally similar compounds.

Lastly, assuming, *arguendo*, that the Examiner had established a *prima facie* under §103, Linn et al. cannot be properly combined with Albers-Schonberg et al. in a manner that teaches or even suggests the instantly claimed compounds because Linn et al. actually teach away from the instantly claimed compounds. A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness (See MPEP §2145). In the instant case, Linn et al. explicitly teach away from the instantly claimed compounds based on the disclosure that both R4 and R5 are hydrogen only when R6 is other than hydroxyl and provided that both R4 and R5 are not simultaneously methyl. Thus, the Examiner has failed to provide a proper rationale for combining the Linn et al. and Albers-Schonberg et al. references.

In view of the foregoing arguments, the Examiner is respectfully requested to withdraw the §103 rejection of claims 1-3, 6 and 7.

Objection to Claims 4-5


Claims 4-5 stand objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants acknowledge the objection and appreciate the Examiner's indication of allowability. Applicants believe, however, the objection is moot due to the allowability of claims 1-3. Withdrawal of the objection of claims 4-5 is respectfully requested.

Conclusion

Present claims 1-7 are allowable over the cited art. Withdrawal of all rejections is respectfully requested, along with issuance of a Notice of Allowance. Applicants invite the Examiner to telephone the undersigned attorney of record if the Examiner feels that the call will be beneficial to advance prosecution of the application.

Respectfully submitted,

Date: July 10 2009
Attorney Docket: 70203


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